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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,976	04/16/2001	David B. Mount	1242/26/2	3961

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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	12

DATE MAILED: 12/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/835,976	MOUNT ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-100* is/are pending in the application.

4a) Of the above claim(s) *1-6,14-58 and 60-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-13 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Action

The examiner in charge of your application in the Patent Office has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Sandra Wegert in Group Art Unit 1647.

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement received 17 August 2001 has been entered into the record. Applicant's election of Invention III, (claims 7-13 and 59) in the Paper sent 27 May 2003 is acknowledged. In addition, Applicant elected the following Group: SEQ ID NO: 15. It should be noted that claims will be examined insofar as they read on the elected Invention. Claims 1-6, 14-58 and 60-100 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim. Applicant elected Invention III with traverse. The traversal is on the ground(s) that the KCC transporters encoded by SEQ ID NO: 5, 7 and 9 should be considered the same invention as the KCC transporter of SEQ ID NO: 15. Applicant's arguments are not persuasive, however, since the SEQ ID NO's in question were properly restricted as separate inventions, each with different functions within cells and within the organism. For example, the Specification makes clear that the selectivity, sensitivity and activity of the KCC transporters are unique for each protein listed (see Figure 8, for example). As further evidence that the KCC transporters are separate inventions, antibodies made against KCC3 demonstrate a lack of cross-reactivity when tested against other KCC transporters (Figure 27D). In addition, since a complete search of the art includes a search of the art that renders an invention obvious as well as anticipatory, the

additional searches required for examination of each additional KCC peptide would be extensive, thus presenting an undue burden for the examiner. The requirement is still deemed proper and is therefore made FINAL.

Claims 7-13 and 59 are under examination in the Instant Application.

Informalities

Specification

The disclosure is objected to because of the following informalities:

URL's

The disclosure is objected to because it contains browser-executable code. This occurs, for example, on page 111, line 14, for example. All URL's should be removed from the Specification. Applicant may refer to web sites by non-executable name only. See MPEP § 608.01 (p).

Appropriate correction is required.

Claim Rejections/Objections

Claim Objections

Claims 7-13 and 59 are objected to for encompassing non-elected inventions (SEQ ID NO: 3-10).

Claim 59 is objected to for depending from a non-elected Claim.

Claim Rejections - 35 USC § 112, first paragraph – scope of enablement.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 7-13 and 59 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO: 15, encoding a KCC3 Potassium-chloride cotransporter, does not enable a polypeptide encoded by a nucleic acid sequence having 75% or more sequence identity to the nucleotide of SEQ ID NO: 15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims.

The specification does not reasonably provide enablement for use of variants of SEQ ID NO: 15 as recited in claims 7-13 and 59. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims recite a nucleic acid having 75% sequence identity to the KCC3 nucleotide of SEQ ID NO: 15. The claims also embrace variants of the SEQ ID NO: 16, such as a *biologically equivalent* polypeptide, or those that are immunologically cross-reactive, or those encoded by a nucleic acid that hybridizes to the first 434 nucleotides of SEQ ID NO: 15.

The instant Application does not reasonably provide enablement for various protein forms of the KCC3 transporter, wherein the protein sequence is encoded by a nucleic acid that is at least 75% identical to the nucleic acid of SEQ ID NO: 15. The specification is not enabling

for the full scope of the claimed nucleotide, wherein the nucleic acid sequence is 75% identical to SEQ ID NO: 15, with the assurance that enabled proteins that are functionally equivalent to SEQ ID NO: 16 can be made without undue experimentation and with the assurance that they would have the desired properties of the claimed KCC3 transporter. There are no examples of what specific polynucleotides fall within the range of those that would be 75% identical. Furthermore, since the claims do not specify a function for SEQ ID NO: 16, requiring only that the variants be the *biological equivalent* of SEQ ID NO: 16, the claims embrace numerous polypeptides with unspecified functions, including those proteins that are structurally dissimilar but serve the same functions within a cell or organism. The specification does not disclose how to use all such variants.

The breadth of claims 7-13 and 59 is too large since the specification fails to provide any guidance on how to produce a nucleic acid which is at least 75% identical to SEQ ID NO: 15 and retains the function of SEQ ID NO: 15. Claims 7-13 and 59 refer to any polynucleotide or polypeptide, that is "at least 75% identical" to that of SEQ ID NO: 15 or 16, without knowledge of the polynucleotides or polypeptides that would fall within this range. In other words, no discussion or working examples, in the instant case, as to what amino acids are necessary to maintain the functional characteristics of the claimed polynucleotide are disclosed. The instant claims suggest altering as much as 25% of the polypeptide disclosed in SEQ ID NO: 16. Although transporter family members share several common structural features, relevant art shows that members of a class having high homology do not always share a specific and substantial functional attribute or utility, despite having structural features in common. Point mutations, for example, serve to illustrate this fact, since a single amino acid mutation can

change the substrate specificity of a transporter or inactivate it (Oelmann, S., et al, 2001., J. Biol. Chem. 28(13): 26291). Bisson, *et al* (1993, Crit Rev Biochem Mol Biol, 28:259) studied yeast transporter knockout phenotypes, and found little correlation between homology and the substrate transported. For example, they found that yeast transporters *Gal2* and *Hxt4* displayed 83.7% homology, but *Gal2* appears to transport Galactose, while *Hxt4* appears to transport Glucose (based on knockout phenotype- compare Table 1 and Table 2A). Similarly, Liang et al found that only a few amino acid substitutions in glucose transporters can change substrate specificity dramatically (1998, Liang, H., et al, Mol. Cell. Biol. 18(2): 926). These examples and others illustrate that it is not predictable as to which amino acids are necessary to maintain the functional characteristics of a protein.

In summary, the specification does not provide a description of a repeatable process of producing, nor of working examples of making the polypeptides whose amino acid sequences deviate from the disclosed sequence (SEQ ID NO: 16) by as much as 25%. In addition, the predictability of the art is low with regards to the knowledge of what effects altering as much as 25% of the sequence of a polypeptide would have on the polypeptide. For this reason, undue experimentation would be required to determine a structure-function relationship for each possible polypeptide encompassed by the claims.

Furthermore, regarding Claims 7-13 and 59, the specification does not enable fragments of SEQ ID NO: 15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims. Claims 7-13 and 59 are directed to the recombinant expression of the

polynucleotide of SEQ ID NO: 15. The scope of the patent protection sought by the Applicant as defined by the claim fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons:

The specific activities of the proteins encoded by the claimed polynucleotide and of any recited peptides that are *immunoreactive with an antibody that is immunoreactive with a polypeptide comprising all or part of the first amino acids of SEQ ID NO: 16* (as recited in Claim 7(e)) are not adequately disclosed. Nor is there disclosed assays to test for these activities. There is no discussion or working examples, disclosed in the instant case, as to what amino acids are necessary to maintain the functional characteristics of the polypeptide encoded by the claimed polynucleotide. Claim 1 encompasses numerous undefined variants that will immunoreact to an antibody made against fragments of SEQ ID NO: 16. However, an antibody developed against a short fragment of SEQ ID NO: 16 will bind an unpredictable number of polypeptides, including possibly those that are dissimilar to the entire length of SEQ ID NO: 16.

Furthermore, regarding Claims 7-13 and 59, the specification does not enable a polypeptide encoded by a nucleic acid molecule capable of hybridizing under *stringent* conditions to a nucleic acid molecule comprising the first 434 nucleotides of SEQ ID NO: 15, as recited in Claim 7(f), for example. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims. The scope of the patent protection sought by the Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons:

The Specification defines *stringent* as the following:

"Stringent temperature conditions will generally include temperatures in excess of about 30°C, typically in excess of about 37°C, and preferably in excess of about 45°C. Stringent salt conditions will ordinarily be less than about 1,000 mM, typically less than about 500 mM, and preferably less than about 200 mM."

The specific activities of the protein encoded by the claimed polynucleotide and of any peptides encoded by the polynucleotides that would hybridize to the claimed polynucleotide, are not disclosed. Nor is there disclosed assays to test for these activities. There is no discussion or working examples, disclosed in the instant case, as to what amino acids are necessary to maintain the functional characteristics of the polypeptide encoded by the claimed polynucleotide. Claim 1 encompasses numerous undefined variants that will hybridize to SEQ ID NO: 15. However, as discussed above, it is not predictable as to which amino acids are necessary to maintain the functional characteristics of a protein.

Due to the large quantity of experimentation required to determine how to use short fragments of SEQ ID NO: 16 as well as variants that would hybridize to SEQ ID NO: 15, the lack of direction or guidance in the specification regarding specific activity of fragments of SEQ ID NO: 16 as well as variants that would hybridize to SEQ ID NO: 15, the lack of working examples to variants of SEQ ID NO: 15 and 16, the state of the art showing the unpredictability of function based on structure, and the breadth of the claims which embrace innumerable fragments of SEQ ID NO: 16 as well as variants that would hybridize to SEQ ID NO: 15, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Claim Rejections- 35 USC § 102

The following are quotations of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-13 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Strausberg, R. (1998, Acc. No. AI313496). Claim 7-13 and 59 encompass a polynucleotide that hybridizes under stringent conditions to a nucleic acid comprising the first 434 nucleotides of SEQ ID NO: 15. Strausberg, R. (1998, Acc. No. AI313496) teaches a DNA that is more than 60% homologous to a polynucleotide that hybridizes under stringent conditions to a nucleic acid comprising the first 434 nucleotides of SEQ ID NO: 15. Since Claims 7-13 and 59 claim sequences that hybridize to the first 434 nucleotides of SEQ ID NO: 15, under the hybridization conditions specified, the polynucleotide cited by R. Strausberg falls within the limits of the claims.

Claims 7-13 and 59 are also rejected under 35 U.S.C. 102(b) as being anticipated by Gu, et al (1996, Accession No. AAA99416). Claims 7-13 and 59 encompass a polynucleotide that includes *part or all* of the first 434 nucleotides of SEQ ID NO: 15. Gu, et al teach an FMR2 polynucleotide that includes part or all of the first 434 nucleotides of SEQ ID NO: 15, since *part or all* can mean very small fragments or even single nucleotides

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claims 7-13 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7-13 and 59 are rendered indefinite because of the phrase "stringent conditions," which is a conditional term. In other words, for example, some nucleic acids which are able to hybridize under stringent conditions would be unable to hybridize under non-stringent conditions. The metes and bounds of the claim, therefore, cannot be ascertained. This rejection can be overcome by supplying specific conditions supported by the specification, which the Applicants consider "stringent," or by removing the indefinite phrase.

Conclusion: Claims 7-13 and 59 are rejected for the reasons recited above.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The

examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

SLW

12/9/03

ELIZABETH KEMMERER
PRIMARY EXAMINER